

The Effect of House Dust Mite Sensitization on Lung Size and Airway Caliber in Symptomatic and Nonsymptomatic Preadolescent Children: A Community-Based Study in Poland

Wiesław Jedrychowski,¹ Umberto Maugeri,² Iwona Jedrychowska-Bianchi,² and Elzbieta Mróz¹

¹Epidemiology and Preventive Medicine, Collegium Medicum, Jagiellonian University, Krakow, Poland; ²Salvatore Maugeri Foundation, Institute for Clinical and Rehabilitation Medicine, Pavia, Italy

There are conflicting reports on the effects of atopy on lung function. The purpose of this study was to compare the effects of house mite (HM) atopy on lung function in subsamples of 12-year-old symptomatic and nonsymptomatic preadolescent children taken from the community sample. An additional objective of this study was to identify possible environmental determinants of HM skin reaction. We obtained questionnaire data on respiratory symptoms and skin-prick tests and performed spirometry on a subsample of 311 children of a birth cohort of children who have been followed over 3 years. Multivariate regression analysis showed progressive decrement of lung function indices (forced vital capacity, forced expiratory volume in 1 sec, and forced expiratory flow, midexpiratory phase) with increasing degree of HM atopy reflected by the skin reaction to HM allergens. The apparent association between the level of HM atopy and the lung function indices was highly significant in symptomatic individuals but insignificant in nonsymptomatic subjects. HM sensitization was significantly associated with mother's atopy. It occurred predominantly in boys and was related to the use of coal or gas for house heating. The effect of allergen sensitization on lung size and airway caliber confined to symptomatic subjects may reflect the inflammatory status of bronchial airways in the symptomatic subjects. **Key words:** children, indoor air quality, lung function, mite atopy, respiratory symptoms. *Environ Health Perspect* 110:571–574 (2002). [Online 15 April 2002] <http://ehpnet1.niehs.nih.gov/docs/2002/110p571-574jedrychowski/abstract.html>

Clough et al. (1) showed that atopic young children with wheezing symptoms or cough displayed lower lung function and suggested that atopy and wheeze are independently associated with respiratory morbidity. Omenaas et al. (2) showed also that allergy to house mites (HM) in adults is an independent predictor of reduced lung function. A significant association between skin test reactivity to HM and decrements in forced expiratory volume in 1 sec (FEV₁) has been observed in children with asthma or frequent wheezing (3,4). Others have found no relationship between FEV₁ level and skin test reactivity to mites or to other allergens in asthmatic patients (5–7). However, a 6-year follow-up study of children in New Zealand demonstrated that those sensitized to HM had a lower FEV₁/percentage forced vital capacity (%FVC) than did the nonsensitized children (8).

The sensitization to HMs and its relation to lung function may be of interest in the context of an intriguing observation by Von Mutius et al. (9,10), who suggested that high outdoor air pollution, especially dust particles, may be protective against atopy.

The purpose of this study was to compare the effects of HM atopy on lung function in subsamples of symptomatic and nonsymptomatic preadolescent children participating in a community-based cohort study in Krakow, Poland. An additional objective of the study was to analyze the

effects of potential environmental determinants of HM skin reactivity such as residence in the polluted inner-city area or indoor air quality characteristics.

Materials and Methods

The subjects of this cross-sectional study were 12-year-old children who participated in the Krakow 3-year prospective cohort study (1995–1998) described elsewhere (11,12). Of 1,044 children taking part in the cohort study, a random sample of 400 children was invited to participate in the atopy study (13); 311 children (response rate, 77.8%) provided respiratory health data, anthropometric and spirometric measurements, and skin prick test results.

Questionnaire. The respiratory health questionnaire collected from mothers contained questions on respiratory symptoms occurring in the last 12 months: cough, phlegm production, wheezing or whistling in chest apart or together with respiratory infections or colds, wheezing with dyspnea, bronchitis spells diagnosed by a physician, and asthma diagnosed by a physician. We considered children symptomatic if they had asthma diagnosed by a physician or complained about wheezing or/and dyspnea attacks with wheezing apart from influenza or colds.

Spirometry. Lung function testing was performed with a Vitalograph computerized spirometer (Vitalograph Ltd., Buckingham

England) on all children by the same technician, who was unaware of the atopy test results or the health status of children assessed by interviewing. We recorded at least three FVC exhalations, which we accepted if measurements were reproducible within 5%. We chose FVC, FEV₁, and forced expiratory flow, midexpiratory phase (FEF_{25–75%}) to assess lung function. FVC is an index of lung volume; FEV₁ is a marker of a functional status of larger bronchial airways; and FEF_{25–75%} is a marker of a functional status of smaller airways. For correct interpretation of lung function indices and prediction of expected normal values, one must consider age, sex, and body size of given subjects (14). Technical details of spirometric measurements have been published elsewhere (11,12). We excluded from the study three children with asthma diagnosed by a physician who were receiving treatment for asthma.

Outdoor air pollution. We based characteristics of the outdoor air pollution in the residence area on communal air pollutants, such as suspended particulate matter (SPM) and sulfur dioxide, measured by the city network of air monitoring stations for the 5 years before the health outcome measurement. In the city center (a highly polluted area), the mean concentration of SPM for the winter season over a 5-year period was 103.5 µg/m³, and the mean concentration of SO₂ was 86.9 µg/m³; the corresponding values in the summer season were 32.3 µg/m³ and 41.8 µg/m³, respectively. In the less polluted area, the mean concentration for the winter season was 45.4 µg/m³ for SPM and 48.4 µg/m³ for SO₂; the corresponding concentrations of air pollutants for the summer season were 16.6 µg/m³ and 28.9 µg/m³, respectively.

Indoor air quality. For indoor air quality assessment, we considered three main variables: environmental tobacco smoke (ETS),

Address correspondence to W. Jedrychowski, Epidemiology and Preventive Medicine, Collegium Medicum, Jagiellonian University, 7 Kopernika Street, Krakow, Poland. Telephone: 48-12-231003. Fax: 48-12-228795. E-mail: myjedryc@cyf-kr.edu.pl

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system of home heating (gas or coal stove vs. central heating), and presence of dampness or mold stains on the apartment walls.

Allergy skin testing. We tested for HM (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and also for common allergens such as grass, grain, and tree pollens and for cat/dog dander before interviewing subjects and performing spirometric examinations. We also administered histamine and phosphate-buffered saline (control). Skin tests were performed on an arm by applying drops of allergen to the arm and pricking the skin under the drops. After 15 min, we measured the length and width of the flare. If the difference between skin reaction to an individual allergen and the flare for the saline control was ≥ 2 mm, we considered the allergic reaction to be positive. A nurse trained in standardized procedures carried out all skin prick testing.

Statistical analysis. We performed the univariate descriptive statistics of lung function by HM atopic status as the first step. We used multivariate linear regression analysis to assess the effect of the degree of HM atopy on lung function adjusted for anthropometric variables and other modifying variables or confounders (sex, bronchitis spells in the last year). Finally, we used a multivariate linear regression model to evaluate the association between the degree of HM atopy and indoor and outdoor air quality variables adjusted for potential confounders (sex of child, parental atopy, and family social status defined by parental education). We used SYSTAT 10 software (15) to perform descriptive and multivariate analyses.

Results

The atopy sample did not differ in characteristics from the cohort study sample except for some excess of children with parental atopy (50% vs. 37.6%). In total, skin allergy was positive (at least to one allergen) in 32.5% of children. The prevalence of allergy was higher in boys than in girls (40.4% vs. 23.8%). The most frequently observed allergies were to grass pollens (18.5%), grain (17.9%), *Dermatophagoides pter.* (16.6%), and *Dermatophagoides far.* (12.0%).

The analysis of individual allergens as predictors of lung function showed significant inverse correlations only between the degree of skin HM (*Dermatophagoides pter.*) reaction and lung function indices.

The 51 children (16.6%) who had a positive HM skin reaction suffered more bronchitis spells and more often lived in houses equipped with coal or gas stoves for heating. This group was more frequently exposed to ETS and more frequently had an atopic mother. The sensitized children, especially those whose allergic weal was ≥ 5 mm, had

lower lung function than did those who tested negative (Table 1).

To assess the interaction between HM allergy and symptoms, we performed analysis of variance for lung function indices (FVC, FEV₁, and FEF_{25-75%}) and for independent variables (asthma symptoms, HM sensitization) and covariables (height and weight). The analysis confirmed significant interaction terms (FVC, $p = 0.13$; FEV₁, $p = 0.03$; FEF_{25-75%}, $p = 0.09$). Given the significant interaction terms between HM allergy and symptoms, we separately analyzed lung function in the symptomatic and nonsymptomatic

children. Besides the weal size, anthropometric characteristics of children (height and weight), sex, and respiratory infections were potential predictors of lung function in the multivariate linear regression models.

Tables 2–4 illustrate the association between pulmonary function level and intensity of atopic skin reaction adjusted for modifiers and confounders. The clear inverse correlation between the degree of HM atopy and the lung function indices was highly significant in symptomatic children but insignificant in nonsymptomatic subjects. In the symptomatic children, HM

Table 1. Characteristics of the study sample and lung function by the house mite sensitization.

	Size of HM skin-prick reaction (mm)				p-Value
	0 (n = 236)	1–2 (n = 22)	3–4 (n = 31)	≥ 5 (n = 19)	
Parental education, university degree (%)	34.7	27.3	38.7	26.3	0.728
Household heating, coal/gas (%)	16.9	27.3	29.0	36.8	0.072
Polluted residence area (%)	46.2	45.5	48.4	57.9	0.798
≥ 2 bronchitis spells in the last year (%)	3.4	13.6	6.5	10.5	0.100
ETS (%)	50.0	54.5	48.4	68.4	0.460
Atopic mother (%)	34.3	27.3	41.9	57.9	0.142
Atopic father (%)	24.0	31.8	12.9	42.1	0.107
Height (cm)					
Mean \pm SD	154.1 \pm 7.51	155.8 \pm 6.14	153.5 \pm 8.41	154.1 \pm 8.33	0.744
Median	155	156	154	154	
Max	174	168	181	168	
Min	128	145	137	141	
Weight (kg)					
Mean \pm SD	45.1 \pm 9.81	50.5 \pm 13.01	44.5 \pm 8.80	46.3 \pm 10.71	0.097
Median	45	48	44	46	
Max	83	81	70	67	
Min	26	35	29	25	
FVC (L)					
Mean \pm SD	2.90 \pm 0.51	3.06 \pm 0.47	2.91 \pm 0.58	2.77 \pm 0.48	0.324
Median	2.87	3.13	2.76	2.70	
Max	4.49	4.12	4.86	3.78	
Min	1.38	2.35	2.07	1.95	
FEV ₁ (L)					
Mean \pm SD	2.58 \pm 0.43	2.65 \pm 0.44	2.55 \pm 0.48	2.37 \pm 0.44	0.165
Median	2.55	2.65	2.48	2.43	
Max	3.81	3.64	4.12	3.23	
Min	1.31	1.83	1.74	1.62	
FEF _{25-75%} (L)					
Mean \pm SD	3.06 \pm 0.65	3.01 \pm 0.76	2.99 \pm 0.69	2.61 \pm 0.73	0.055
Median	3.05	3.00	2.95	2.50	
Max	5.80	4.58	4.55	3.81	
Min	1.39	1.32	1.84	1.24	

Table 2. Multiple linear regression of FVC on sex, height, weight, bronchitis spells, and weal size in nonsymptomatic and symptomatic children.

	β Coefficient	β SE	t-Value	p-Value
Nonsymptomatic children (n = 250)				
Sex ^a	–0.173	0.040	–4.365	0.0000
Height (cm)	0.616	0.053	11.636	0.0000
Weight (kg)	0.234	0.053	4.446	0.0000
HM weal size (mm)	–0.047	0.039	–1.191	0.2365
Bronchitis ^b	0.060	0.039	1.546	0.124
Symptomatic children (n = 58)				
Sex ^a	–0.025	0.070	–0.350	0.7280
Height (cm)	0.688	0.087	7.881	0.0000
Weight (kg)	0.269	0.086	3.114	0.0030
HM weal size (mm)	–0.184	0.068	–2.731	0.0086
Bronchitis ^b	–0.064	0.065	–0.972	0.3355

For symptomatic children, $R = 0.89$, $R^2 = 0.79$.

^a0 = boys; 1 = girls. ^b0 = 0 or 1 bronchitis spell; 1 = ≥ 2 bronchitis spells over the last year.

weal size and FVC correlated inversely (β coefficient = -0.184 ; $p = 0.009$), whereas in the nonsymptomatic children the association was insignificant (β coefficient = -0.047 ; $p = 0.237$). The same pattern emerged for FEV₁ and for FEF_{25-75%}. Thus, the data clearly demonstrated that the effect of the HM weal size was inversely associated with lung function among those children who were symptomatic. In nonsymptomatic children, the association between HM sensitization and lung function was insignificant.

In the final stage of the analysis, we considered the association between HM sensitization and outdoor and indoor air

quality adjusted for potential confounders such as sex of child, parental education, or parental atopy in the total study sample. The analysis shows that of the considered environmental factors, only house heating system appeared to be highly significant (β coefficient = -0.190 ; $p = 0.001$). The children from houses heated by gas or coal showed stronger HM skin reaction than did those with central heating (Table 5). Neither ETS nor high air pollution in the residence area or molds or house humidity showed a significant correlation. The sensitization scores were higher in boys than in girls, and we observed a clear association

between degree of HM sensitization in children and mother's atopy (β coefficient = 0.145 ; $p = 0.009$).

Discussion

Our data show significant inverse associations between HM atopy, lung size, and function of large and small airways in children. Only symptomatic children showed a progressive decrement of pulmonary function level with increasing degree of HM atopy, as reflected by the skin weal size in reaction to mite allergens. This suggests that HM weal size may be a marker of inflammatory status of airways. This finding has important biologic significance because sensitized children may achieve lower levels of lung function in early adulthood and have a more rapid decline in lung function in later life. This is an additional argument in the discussion about treating children with HM skin allergy as a high-risk group that may experience high vulnerability to environmental hazards.

Cockcroft et al. (16) demonstrated that the pulmonary response to an inhaled allergen is a function of three factors: *a*) the underlying degree of bronchial responsiveness, *b*) the level of allergen in the environment, and *c*) the degree of sensitization as measured by the allergic skin reactivity. We have not analyzed the interrelationship between lung function, bronchial reactivity, and atopy because our study focused only on skin test reactivity and decrements in pulmonary function. We did not measure bronchial responsiveness or actual antigen levels in the household environment.

Other indoor allergens (dander of dogs/cats) had no significant effect on lung function decrement, but this might be attributed to a low number of pet owners in the study sample.

To a great extent, our study is in agreement with results published by Henderson et al. (17), who found increased specific immunoglobulin E scores correlated with lower pulmonary function in the small airways of boys who had two or more wheezing episodes in the preschool years. However, we found no such correlation in girls, or in boys with one or no episodes of wheezing. Schwartz and Weiss (3) also observed a significant association between skin test reactivity to HM and decrements in FEV₁ in a random sample of children with asthma or frequent wheezing. In their study, variation in peak expiratory flow was also associated with the degree of skin sensitivity to common allergens. In contrast, Cline et al. (6) found no relationship between FEV₁% and skin test reactivity to HM or to other allergens.

The conflicting reports on the effects of atopy on lung function may be due to various selection methods of study groups.

Table 3. Multiple linear regression of FEV₁ on sex, height, weight, bronchitis spells, and weal size.

	β Coefficient	β SE	t-Value	p-Value
Nonsymptomatic children (n = 250)				
Sex ^a	-0.051	0.0449	-1.135	0.2575
Bronchitis ^b	0.043	0.044	0.976	0.3302
HM weal size (mm)	-0.073	0.044	-1.652	0.0999
Height (cm)	0.609	0.060	10.130	0.0000
Weight (kg)	0.161	0.060	2.689	0.0077
Symptomatic children (n = 58)				
Constant	—	—	-4.454	0.0000
Sex ^a	0.015	0.080	0.183	0.8553
Bronchitis ^b	-0.162	0.075	-2.169	0.0347
HM weal size (mm)	-0.268	0.077	-3.474	0.0010
Height (cm)	0.637	0.099	6.369	0.0000
Weight (kg)	0.261	0.099	2.638	0.0109

For symptomatic children, $R = 0.86$, $R^2 = 0.74$.

^a0 = boys, 1 = girls. ^b0 = 0 or 1 bronchitis spell; 1 = ≥ 2 bronchitis spells over the last year.

Table 4. Multiple linear regression of FEF_{25-75%} on sex, height, weight, bronchitis spells, and weal size in nonsymptomatic and symptomatic children.

	β Coefficient	β SE	t-Value	p-Value
Nonsymptomatic children (n = 250)				
Sex ^a	0.159	0.059	2.680	0.0079
Bronchitis ^b	-0.017	0.058	-0.291	0.7717
HM weal size (mm)	-0.065	0.059	-1.106	0.2697
Height (cm)	0.367	0.079	4.627	0.0000
Weight (kg)	0.004	0.079	0.055	0.9559
Symptomatic children (n = 58)				
Constant	—	—	-1.087	0.2823
Sex ^a	0.028	0.125	0.220	0.8271
Bronchitis ^b	-0.255	0.117	-2.184	0.0335
HM weal size (mm)	-0.304	0.121	-2.522	0.0148
Height (cm)	0.333	0.156	2.134	0.0376
Weight (kg)	0.190	0.154	1.231	0.2239

For symptomatic children, $R = 0.60$, $R^2 = 0.36$.

^a0 = boys, 1 = girls. ^b0 = 0 or 1 bronchitis spell; 1 = ≥ 2 bronchitis spells over the last year.

Table 5. Multiple linear regression of HM weal size on potential determinants.

	β Coefficient	β SE	t-Value	p-Value
Constant	—	—	2.922	0.0037
Sex ^a	-0.181	0.055	-3.304	0.0011
ETS ^b	0.0580	0.056	1.044	0.2976
Parental education ^c	0.0168	0.055	0.304	0.7612
House heating method ^d	0.190	0.056	3.410	0.0007
Molds or water stains on walls ^e	-0.048	0.056	-0.857	0.3921
Atopic mother ^f	0.145	0.055	2.635	0.0088
Atopic father ^f	-0.024	0.055	-0.437	0.6622

$R = 0.31$, $R^2 = 0.09$; $n = 308$.

^a0 = boys, 1 = girls. ^b0 = negative ETS, 1 = positive ETS. ^c0 = at least one of the parents received medium level education, 1 = at least one of the parents received grammar school education. ^d0 = central heating, 1 = gas or coal oven within the household for heating. ^e0 = no water stains or fungi seen on the walls, 1 = water stains or fungi seen on the walls. ^f0 = no allergy, 1 = presence of asthma or skin allergy.

Moreover, some of the studies dealt only with clinical series, and up to now, there is a lack of data that compare the effects of atopy on lung function in symptomatic and nonsymptomatic children in community-based studies.

The analysis of our data has demonstrated that of the environmental factors taken into consideration, only indoor air quality—but not outdoor air quality—appears to be significantly related to HM sensitization. The children from houses heated with gas or coal showed stronger HM skin reaction than did those from houses with central heating. ETS, high air pollution in the residence area, and house molds and humidity showed no significant correlation. We found a clear association between HM sensitization in children and in mother's but not father's atopy. It is difficult to explain the association between coal or gas used for heating and HM sensitization. This variable may simply indicate houses with higher allergen levels. Two studies have shown that the concentration of allergens is well correlated with the degree of sensitization (18,19).

We based our study on relationship between HM sensitization and lung function on the cross-sectional approach, and some inherent flaws in this study design could weaken the evidence in question. First of all, we did not have data on the onset and duration of atopy in the past. Therefore, we could not assess the sequence and timing of

causal events and health outcomes (lung function deterioration). However, the consistent and strong dose–effect correlation between the degree of HM sensitization and lung function supports the causal relationship. The children under study were not fully representative of the cohort sample. In the atopy study, children with atopic parents were overrepresented, but we accounted for the potential confounding effect of parental atopy in the multivariate analysis.

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